REMARKS

The Present Invention

The present invention pertains to a method for obtaining gene expression in somatic cell tissue and a method for immunization, by administering a plasmid expression vector using a jet injector.

The Pending Claims

Claims 1-12 and 19-23 are currently pending, of which claims 1-12, 19, 20, 22 and 23 are directed to the method for obtaining gene expression in somatic cell tissue, and claim 21 is directed to the method for immunization.

The Office Action

Claims 1-12 and 19-23 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. Claim 5 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Reconsideration of these rejections is hereby requested.

Amendments to the Claims

Claims 13-18 have been canceled as directed to non-elected subject matter. Claim 2 has been amended to recite "by transient expression of the plasmid expression vector" as supported by the specification at, for example, page 3, line 29, and page 4, line 25, in an effort to advance prosecution and not in acquiescence of any rejection set forth in the final Office Action. Claim 5 has been amended to delete "which are combined to directly express in a specific manner" in an effort to advance prosecution and not in acquiescence of the rejection. No new matter has been added by way of these amendments.

Discussion of Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-12 and 19-23 have been rejected under Section 112, first paragraph, for allegedly lacking enablement. The Office agrees that the claimed invention is enabled for methods of gene transfer for non-therapeutic purposes and for genetic immunization. The Office, however, alleges that the specification does not enable the methods embodied in groups "(a)", "(b)", and "(i)" of claim 2. This rejection is traversed for the reasons set forth below.

The Office alleges that the ablation of cells, as recited in groups "(a)" and "(b)" is not enabled by the specification. Applicants respectfully submit that cellular ablation via jet-injection of vector constructs does not suffer from the technical difficulties alleged by the Office. Specifically, the present invention provides for the direct localization of vector to the target site via jet-injection to specific tissue. Furthermore, the specification evidences the successful targeting of nucleic acids to somatic tissue (mammary gland) via jet injection by

way of the CAT and β-gal gene delivery and expression data at, for example, pages 10-12. As long as the specification discloses at least one method for making and using the claimed invention, then the enablement requirement of 35 U.S.C. § 112 is satisfied. *See In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970).

Yet the Office contends that the claimed method of cellular ablation encompasses stable expression of a construct. Based on such a contention, the Office further contends that the specification does not enable stable expression. Contrary to what is contended by the Office, undue experimentation would not be required to practice such methods in view of the data presented in the specification and given the knowledge in the art at the time of the present invention as to how to manipulate a vector to achieve prolonged or sustained expression of a gene contained within the vector. With that said, Applicants point out that an agent that ablates a cell would only, be transiently expressed, irrespective of whether the construct is one that is capable of being stably expressed, inasmuch as expression of such an agent results in the destruction of the cell. Any agent that is capable of ablating a cell would be expected to have an immediate effect.

In an effort to advance prosecution and not in acquiescence of the rejection, Applicants have amended claim 2 to recite "by transient expression of the plasmid expression vector" with respect to (a) and (b).

The Office also alleges that the specification does not enable a method of inducing wound healing. Specifically, the Office states that there is no distinction between inducing an event and causing an event. Furthermore, the Office alleges that, without a therapeutic use for the claim, no utility is apparent. Lastly, the Office states that "inducing wound healing" encompasses methods of gene therapy. Applicants submit that group (i) of claim 2 enables a method for inducing healing.

Applicants assert that the term "inducing" and the term "causing" have different meanings, and cannot be substituted for one another in the context of the present invention. Group "(i)" recites a method for "inducing" healing, not a method for healing per se. The Merriam-Webster Dictionary Online defines "inducing" as *bringing about by stimulation.* Additionally, the term "causing" is defined as *bringing about a result.* For example, a catalyst for a chemical reaction induces the reaction, but it is not the proximate cause of the resulting reaction. The proximate cause of the reaction is the reactants. In this same regard, the present invention induces or stimulates wound healing, but it is not the proximate cause of the healing of the wound. Therefore, the specification need only enable a therapeutic method to stimulate healing--not the healing, itself. As such, the administration of exogenous DNA via jet injection will induce an immune response, which in turn, can induce healing, as evidenced by the art. *See* Chen et al. *Zhonghua Zheng Xing Shao Shang Wai Ke Za Zhi*, May 1999; 15(3):170-172 (abstract enclosed herein). Furthermore, the method of group (i) does not encompass gene therapy as alleged by the Office, for the same reasons that groups (a) and

(b) do not disclose methods relating to gene therapy. Thus, the disclosure of the instant application enables group "(i)". However, in an effort to advance prosecution and not in acquiescence of the rejection, Applicants have amended claim 2 to recite "the transient expression of a growth factor" with respect to (i).

In view of the foregoing, Applicants submit that claims 1-12 and 19-23 are enabled. Accordingly, Applicants respectfully request withdrawal of the rejection under Section 112, first paragraph.

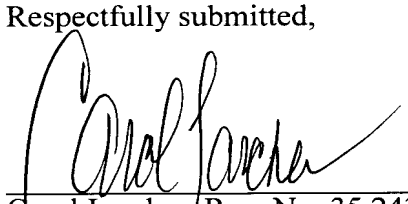
Discussion of Rejection under 35 U.S.C. § 112, second paragraph

Claim 5 has been rejected under Section 112, second paragraph, as allegedly indefinite for failing to point out particularly and claim distinctly the subject matter of the invention. The rejection is believed to be moot in view of the amendment to the claim..

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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1: Zhonghua Zheng Xing Shao Shang Wai Ke Za Zhi. 1999 May;15(3):170-2.

Related Articles
Link

[Effects of PCMV4-hTGF beta 1 as nucleic acid vaccine on II* burn wound healing and postburn scarring in rats]

[Article in Chinese]

Jia C, Chen B, Wang D.

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OBJECTIVE: To investigate the gene expression of PCMV4-hTGF beta 1 as nucleic acid vaccine regulation and the effects on burn wound healing and scarring in rats and study the feasibility of gene therapy in burns.
METHODS: Sixty wistar rats were divided into three groups: 1. burn + nucleic acid vaccine; 2. nucleic acid vaccine only(control); 3. burn only (control). ELISA was used to determine the dynamic changes in anti-TGF beta 1 neutralizing antibody in serum; determination of the quantities of DNA retained in muscles by Southern blot and in situ hybridization; observation of the ratio in collagen I/III during the wound healing by special stain method.
RESULTS: The level of anti-TGF beta 1 antibody in serum reached the peak at the third week after naked DNA was injected, and a slight drop in the 4th week. TGF beta 1 plasmid DNA could be detected 5 minute after injection, and lasted 3 hours. In situ hybridization showed a positive staining in muscle fibers 5 days after injection. During the day 0-day 9, the wound healing speed in vaccine group was faster than control, and after day 10, no significant difference was found between groups, but the ratio of collagen I/III was reduced remarkably in vaccine group. CONCLUSION: Injection of PCMV4-hTGF beta 1 in rats can really cause general immune response reaction. It wa showed that PCMV4-hTGF beta 1 was similar to TGF beta 1, and it had the effect of stimulating of epidermic cells to accelerate wound healing at early stage, and at later stage, it was similar to anti-TGF beta 1 neutralizing antibody, having the effect of inhibiting hyperplasia of scar. So it is confirmed that PCMV4-hTGF beta 1 as nucleic acid vaccine has the effect of promoting healing of burn wound and controlling the formation of scar.

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